

CORRECTED VERSION

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
11 November 2004 (11.11.2004)

PCT

(10) International Publication Number
WO 2004/096807 A3

(51) International Patent Classification⁷: **C07D 487/04**,
471/04, A61K 31/4985, A61P 31/18

(21) International Application Number:
PCT/EP2004/050621

(22) International Filing Date: 27 April 2004 (27.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/465,987 28 April 2003 (28.04.2003) US
03101164.6 28 April 2003 (28.04.2003) EP

(71) Applicant (for all designated States except US): **TI-
BOTEC PHARMACEUTICALS LTD.** [IE/IE]; Little
Island, Co Cork (IE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **VERSCHUEREN**,
Wim, Gaston [BE/BE]; De Wittestraat 5, B-2600

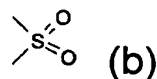
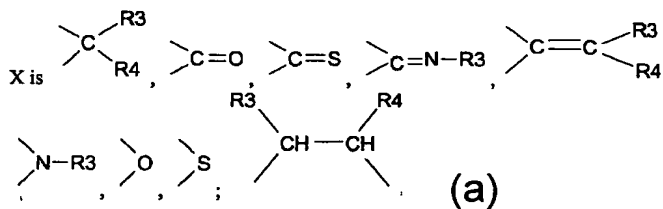
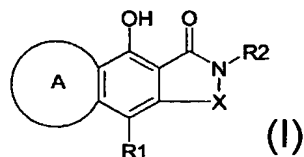
Berchem (BE). **DIERYNCK, Inge** [BE/BE]; Moonsstraat
38, B-2018 Antwerpen (BE). **SURLERAUX, Dominique**,
Louis, Nestor, Ghislain [BE/BE]; Rue de la Scaillée 13,
B-1440 Braine-le-Château (BE). **DAEYAERT, Frederik**,
Frans, Desiré [BE/BE]; Stijn Streuvelsstraat 64, B-2340
Beerse (BE).

(74) Agent: **DAELEMANS, Frank**; Tibotec-Virco Comm.
VA, Generaal De Wittelaan L11 B3, B-2800 Mechelen
(BE).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

[Continued on next page]

(54) Title: HIV INTEGRASE INHIBITORS



(57) Abstract: The present invention concerns the compounds having the formula (I), N-oxides, salts, stereoisomeric forms, racemic mixtures, prodrugs, esters and metabolites thereof wherein (a) or (b); A, together with the two carbons of the phenyl ring to which it is attached forms a monocyclic aryl or a monocyclic Het²; R¹ is hydrogen, halo, nitro, cyano, sultam, sultim, C₃₋₇cycloalkyl, C(=O)-R⁵, S(=O)₂-R⁶, OR⁷, NR⁸R⁹, C(=NR⁸)-R⁵, optionally polysubstituted C₁₋₆alkyl, optionally polysubstituted C₂₋₆alkenyl or optionally polysubstituted C₂₋₆alkynyl; R² is hydrogen, C₃₋₇cycloalkyl, aryl, Het¹, Het², C(=O)-R⁵, S(=O)₂-R⁶ OR⁷, NR⁸R⁹, C(=NR⁸)-R⁵, or optionally polysubstituted C₁₋₆alkyl, optionally polysubstituted C₂₋₆alkenyl or optionally polysubstituted C₂₋₆alkynyl. It further relates to their use as HIV integrase inhibitors, processes for their preparation as well as pharmaceutical compositions and diagnostic kits comprising them. It also concerns combinations thereof with other anti-retroviral agents, and to their use in assays as reference compounds or as reagents.



(84) **Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
— of inventorship (Rule 4.17(iv)) for US only

Published:

— with international search report
— with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

(88) **Date of publication of the international search report:**
6 January 2005

(48) **Date of publication of this corrected version:**
22 September 2005

(15) **Information about Correction:**
see PCT Gazette No. 38/2005 of 22 September 2005, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.